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Effect of Erythrocytapheresis on Arterial Oxygen Saturation and Hemoglobin Oxygen Affinity in Patients With Sickle Cell Disease

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An important purpose of blood transfusion in patients with sickle cell disease is to improve arterial oxygen saturation (SaO_2) and thereby reduce red cell sickling. To investigate the degree of improvement in SaO_2 by blood transfusion, we determined the hemoglobin oxygen affinity, transcutaneous oxygen saturation ($Tc\text{-}SO_2$), and pulse rate before and after automated partial exchange transfusion (erythrocytapheresis). In 13 patients with sickle cell disease who underwent 24 erythrocytapheresis procedures, the mean oxygen tension at half saturation (P50) was significantly reduced from 30.4 ± 2.2 to 26.0 ± 1.6 mm Hg ($P < 0.01$) immediately after exchange transfusion. Mean $Tc\text{-}SO_2$ values increased from 96.2 ± 2.8 to 98.5 ± 2.1% ($P < 0.01$). Approximately 50% of the increase in $Tc\text{-}SO_2$ after erythrocytapheresis could be explained by the increase in hemoglobin oxygen affinity. An increase in arterial oxygen pressure (PaO_2) following erythrocytapheresis, suggested by the calculated PaO_2 in this study, may explain some of the increase in $Tc\text{-}SO_2$. We conclude that improvement in $Tc\text{-}SO_2$ in patients with sickle cell disease resulted from changes in hemoglobin oxygen affinity as well as blood oxygen pressure following erythrocytapheresis. Am. J. Hematol. 59:5–8, 1998.

Key words: transcutaneous oxygen saturation; sickle cell disease; partial exchange transfusion; erythrocytapheresis; pulse oximeter; P50; calculated PaO_2

INTRODUCTION

Previously, we reported that transcutaneous oxygen saturation differs between patients with sickle cell disease (SCD) and normal subjects [1]. Patients with SCD often have a lower arterial oxygen pressure (PaO_2) than normal subjects [1–3]. Since hemoglobin oxygen dissociation curves (ODC) in patients with SCD are shifted toward the right, a relatively small fall in PaO_2 usually results in a significant reduction in oxygen saturation [3,4]. This study was designed to examine the changes in arterial oxygen saturation (SaO_2), pulse rate, and P50 values (partial pressure of oxygen at which 50% of the hemoglobin is saturated with oxygen) that would occur after erythrocytapheresis in patients with sickle cell disease. Studies on hemoglobin oxygen affinity of stored blood have shown a markedly reduced P50 value, resulting from the low level of 2,3-diphosphoglycerate (DPG), which begins 7 days following blood collection [5,6]. Erythrocytapheresis using blood stored for 7 days or more after collection, therefore, should shift ODC of the recipient's blood to the left. We hypothesized that this shift in ODC in transfused patients could be detected

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TABLE I. Patient Data: Pre- and Post-Erythrocytapheresis Hb A and Hb S Levels*

Patient no.	Age (year)	Sex	Hb A	Hb S
1.	20	M	77	23
			54	46
2.	14	F	60	40
			62	38
3.	21	M	71	29
			60	40
			58	42
4.	20	M	57	43
			55	45
5.	16	F	55	45
6.	24	M	76	24
			55	45
			47	53
7.	26	M	45	55
			53	47
8.	15	M	80	20
9.	10	M	96	4
			72	28
10.	23	M	48	52
11.	28	F	59	41
			55	45
12.	15	M	70	30
			57	43
13.	11	M	32	68
Mean ± SD	18.7 ± 5.7		60.5 ± 13.4	39.5 ± 3.5

*Hb, hemoglobin; M, male; F, female.

from the change in transcutaneous oxygen saturation ($Tc\text{-}SO_2$), as measured by pulse oximetry. We measured $Tc\text{-}SO_2$ pre-, intra-, and post-erythrocytapheresis in patients with SCD to determine whether changes in SaO_2 reflect changes in the affinity of hemoglobin for oxygen.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board of The Children's Hospital of Philadelphia. Informed consent was obtained from all patients and/or parents prior to study enrollment. No patient was given supplemental oxygen during the study. Hb S levels before and after erythrocytapheresis were determined by the cellulose acetate electrophoresis/densitometry method (Table I). The volume of packed RBCs required for erythrocytapheresis was determined to reduce the pre-exchange Hb S level by 50 to 60% at the end of the erythrocytapheresis. $Tc\text{-}SO_2$ was measured with a pulse oximeter (N-200, Nellcor, Inc., Hayward, CA) immediately prior to and following erythrocytapheresis and during the erythrocytapheresis following transfusion of each unit of packed red blood cells (P-RBC). Pulse rates were measured before venipuncture and during and after erythrocytapheresis. Peripheral venous blood samples were drawn before erythrocytapheresis. The ODC of red blood cell suspensions from patients and donor RBC units were determined at pH 7.4 and 37°C with a Hemox Analyzer (Technical Consulting Service, Southampton, PA) as previously described [6,7]. P50 measurements were standardized for hemoglobin concentration. Specimens were preserved in EDTA and kept on ice until assayed; measurements were performed within 4 h of specimen collection. Concentrations of 2,3-DPG in whole blood from patients and samples from donor RBC were determined using a Sigma diagnostic kit 35-UV (Sigma Chemical Company, St. Louis, MO). PaO_2 was calculated from the patients' oxygen dissociation curves and $Tc\text{-}SO_2$ values. Calculated SaO_2 was derived from the patients' post-exchange ODC and calculated pre-exchange PaO_2.

Automated erythrocytapheresis was performed with the Haemonetics V50 Plus blood cell separator (Haemonetics Corp., Braintree, MA) using a pediatric bowl (apheresis set no. 11010) [8]. Each cycle consisted of removal of about 150 mL of blood followed by replacement of approximately an equal volume of donor RBC with the autologous plasma that was separated during the draw cycle. The cycle was then repeated until about 50–60% of the patient's original circulating RBCs were exchanged. The erythrocytapheresis procedure was completed in about 90–120 min. For the procedure, 4- to 9-day-old CPD- or CPDA-1 stored RBC with a hematocrit of approximately 75% was used. In patients with a history of non-hemolytic febrile transfusion reactions, washed leukocyte-poor RBCs were used. Blood volume was estimated from the body weight using a formula of 70–75 mL/kg.

Data are reported as mean ± standard deviation. Paired Students' *t*-tests, Student-Newman-Keuls test, and linear regression analyses were used for statistical evaluation of the data.

RESULTS

Twenty-four erythrocytapheresis procedures were performed in 13 patients with SCD who had had stroke and were on chronic transfusion therapy. There were 10 male and 3 female patients, aged 10 to 28 years (mean, 18.6 ± 5.5 years). All patients were in their usual state of health without acute chest syndrome or vaso-occlusive crisis at the time of erythrocytapheresis. In 16 of the 24 exchanges, 3 U of RBC (700–800 ml) were used as replacement RBC, while 4 U (800–1,100 ml) were used in the remaining eight procedures. The percentages of Hb A and Hb S before erythrocytapheresis were 60.5.4 ± 13.4% and 39.5 ± 3.5%, respectively (Table I). Pre- and post-exchange transfusion P50, calculated PaO_2, 2,3-DPG, pulse rate, $Tc\text{-}SO_2$, and calculated SaO_2 values are shown in Table II.

TABLE II. Comparison of Mean Pre- and Post-Transfusion P50, Calculated PaO_2, 2,3-DPG, Pulse Rate, Tc-SO_2, and Calculated SaO_2 Values in Patients With Sickle Cell Disease*

	n	Pre-PExT	Post-PExT	*P*	Mean pre- vs. post-PExT difference	Change (%)
P50 (mm Hg)	24	30.4 ± 2.2	26.0 ± 1.6	<0.01	4.4 ± 1.4	14.2 ± 4.2
Calculated PaO_2 (mm Hg)	24	76.0 ± 11.0	85.8 ± 11.2	<0.01	10.0 ± 8.7	14.1 ± 13.0
2,3-DPG (nmol ml^{-1} RBC)	19	6,109.5 ± 833.2	4,667.4 ± 456.2	<0.01	1,442 ± 732	22.6 ± 10.0
Pulse rate (min^{-1})	24	77.9 ± 11.6	76.5 ± 12.3	NS	1.3 ± 7.7	1.9 ± 0.3
Tc-SO_2 (%)	24	96.2 ± 2.8	98.5 ± 2.1	<0.01	2.3 ± 2.1	2.4 ± 2.2
Calc. SaO_2 (%)	24	97.0 ± 2.3	—	—	—	—

*P50, partial oxygen pressure at which 50% of the hemoglobin is saturated with oxygen; Calculated PaO_2, PaO_2 derived from Tc-SO_2 and patient's oxygen dissociation curve; 2,3-DPG, 2,3-diphosphoglycerate; PExT, partial exchange transfusion; Tc-SO_2, transcutaneous oxygen saturation, as measured by pulse oximeter; Calc. SaO_2, SaO_2 derived from the post-transfusion ODC and pre-transfusion Calc. PaO_2. Values represent the mean ± SD.

Oxygen Affinity of Red Blood Cells

The mean values for P50 and 2,3-DPG of units of donor RBC were 17.3 ± 2.1 mm Hg and 1,483.8 ± 736.5 nmol ml^{-1} RBC, respectively. There were no significant differences in hematocrit, P50, and 2,3-DPG concentrations among the donor RBC units. P50 and 2,3-DPG levels decreased significantly ($P < 0.01$) in all patients following erythrocytapheresis (Table II). The mean difference between the pre- and post-erythrocytapheresis P50 values was significant ($P < 0.01$).

Transcutaneous Oxygen Saturation

Mean Tc-SO_2 values prior to erythrocytapheresis, during the procedure following replacement of each donor RBC unit, and after the procedure are shown in Table III. Tc-SO_2 increased gradually during erythrocytapheresis, with a significant increase following replacement of each unit of RBC except for the first unit. This increase was greatest in those patients with the lowest pre-exchange Tc-SO_2. There was no significant correlation between Tc-SO_2 and P50 in these patients, either prior to or after erythrocytapheresis.

In most patients, the calculated PaO_2 rose after erythrocytapheresis. Three patients demonstrated a decrease in their calculated PaO_2, but the decrease was less than 3% in two of these patients. Following erythrocytapheresis, the mean Tc-SO_2 and calculated SaO_2 were 98.6 ± 2.1 and 97.1 ± 2.3% ($P < 0.05$), respectively. The proportion of the change in Tc-SO_2 explained by change in the ODC was calculated as follows: (pre-transfusion Tc-SO_2 post-transfusion Tc-SO_2)/(pre-transfusion Tc-SO_2) post-transfusion calculated SaO_2). The mean proportion was 0.47 ± 0.54.

Pulse Rate

There was no significant correlation between the pre- and post-exchange difference in pulse rate and the P50, or correlation between the pre- and post-exchange difference in pulse rate and concentration of 2,3-DPG. The mean differences in calculated blood volume and the percent change in blood volume before vs. after erythrocytapheresis were 174.4 ± 112.1 ml and 4.6 ± 2.7%, respectively. No significant correlation was found between the pre- and post-transfusion difference in pulse rate and the percent change in blood volume.

DISCUSSION

Although there have been questions regarding the use of Tc-SO_2 in patients with SCD [9,10], Weston Smith et al. [4] and Rackoff et al. [1] have demonstrated the accuracy of Tc-SO_2 in patients with SCD, when the differences in patients' ODC were taken into account. Therefore, transcutaneous SaO_2 was considered to accurately reflect the true SaO_2 in this study. The mean Tc-SO_2 in the patients prior to erythrocytapheresis in this study was 96.2 ± 2.8%, a relatively high value [2,11], and the mean P50 was 30.4 ± 2.2 mm Hg, a relatively low value for patients with SCD [6,12]. The reason may be that patients were being maintained on chronic erythrocytapheresis therapy, and have higher baseline Hb levels than non-transfused patients, which reduces the level of 2,3-DPG. A low 2,3-DPG level shifts the ODC to the left, which has a tendency to increase the SaO_2.

The Tc-SO_2 level rose gradually during erythrocytapheresis in this study, suggesting that increases in Tc-SO_2 are the result of erythrocytapheresis. Following erythrocytapheresis, Tc-SO_2 was higher than the calculated SaO_2, which was derived from the patients' post-erythrocytapheresis ODC and pre-exchange Tx calcu-

TABLE III. Mean Tc-SO_2 Values During Erythrocytapheresis*

	n	Tc-SO_2 (%)	*P* (vs. Pre-PExT)
Pre-PExT	24	96.2 ± 2.8	
1st unit	23	97.0 ± 2.5	NS
2nd unit	24	97.6 ± 2.3	<0.01
3rd unit	23	98.0 ± 2.2	<0.01
Post-PExT	24	98.5 ± 2.1	<0.01

*NS, not shown.

lated PaO_2. In this study, we used the pre-exchange Tx calculated PaO_2 for the calculation of post-exchange Tx SaO_2 to determine the change in SaO_2, which was due solely to the increase in oxygen affinity. Approximately 50% of the increase in Tc-SO_2 could be explained by the increase in hemoglobin oxygen affinity.

One reason for the increase in Tc-SO_2 is the increase in PaO_2 following erythrocytapheresis, as reported by Lanzkowsky et al. [13]. They have shown that sickle cell patients with acute chest syndrome demonstrate remarkable improvement in PaO_2 levels following erythrocytapheresis, and they speculated that the increase in PaO_2 was due to an improvement of pulmonary microcirculation. At the equivalent hematocrit, Hb S blood is more viscous than hemoglobin A (Hb A) blood [14], and mixtures of Hb A and Hb S blood have better flow properties than Hb S blood alone [15]. Thus, decreased viscosity following erythrocytapheresis, which reduces the number of sickle cells, could lower peripheral resistance in the pulmonary circulation as well as in the systemic circulation. The improvement in pulmonary circulation may reduce ventilation-perfusion mismatching and intrapulmonary shunting, which are thought to cause a low PaO_2 in SCD [2,11], thus increasing the PaO_2.

An increase in blood flow to the skin following erythrocytapheresis also may affect Tc-SO_2. LaCelle [16], using a muscle capillary system, has demonstrated that deoxygenation of transfused sickle cells causes a progressive 2–3-fold increase in flow resistance, with subsequent stasis. This microvascular flow disturbance would decrease Tc-SO_2 and result in a discrepancy between Tc-SO_2 and SaO_2. However, other reports demonstrating the accuracy of Tc-SO_2 in SCD suggest that microvascular flow disturbances in sickle cell patients exert little effect on Tc-SO_2 because there is close agreement between these two parameters [1,4]. Therefore, the increase in microvascular flow following erythrocytapheresis would have little effect on Tc-SO_2.

We conclude that patients with sickle cell disease show an improvement of transcutaneous oxygen saturation following erythrocytapheresis and that this improvement indicates an increase in hemoglobin oxygen affinity as well as an improvement in arterial oxygen pressure.

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